UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,765	10/02/2003	George N, Serbedzija	018852-000511US	1627

20350 7590 06/01/2009

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
06/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,765	SERBEDZIJA ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/07/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,33,35-40 and 42-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,33,35-40 and 42-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/07/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/07/2009 has been entered.

Claims 31 and 42 are amended. Claims 31,33,35-40,42-57 are pending and under consideration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 31,33,35-40,42,54 and 56 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 7,435,870. Although the conflicting claims are not identical, they are not patentably distinct from each other because detection of toxic activity as claimed in the parent embraces screening for both toxic and pharmacological activity as claimed as a toxic activity can be considered to be pharmacological.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) was denied as set forth at page 4 of the office action dated 08/03/2006. The effective filing date granted for the claims is **02/22/1999** based on support in US Application 09/255,397. '783 does not provide support for screening compounds by assaying for gene expression changes. Applicant has remarked that the issue of priority does not currently appear to be material to the grounds of rejection raised and will further address the issue if it becomes relevant in future proceedings.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 31,33, 35-38,54 and 56 under 35 U.S.C. 112, first paragraph, is withdrawn in light of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 42-46 and claims 53 and 57 under 35 U.S.C. 102(b) as being anticipated by Mizell [1997, IDS] is withdrawn in light of Applicant's Applicant's amendments to the claims. However, a new rejection under 35 USC 103 is set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

.1) Claims 42-46,53 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizell [1997, IDS] as evidenced by Blader (1998, Developmental Biology, 201:185-201)

As set forth above, priority to US provisional applications 60/075,783 and 60/100,950 for the instantly claimed subjected matter has been denied. The effective filing date is 02/22/1999.

The teachings of Mizzel are applied to the claims as set forth at page 7 of the office action dated 02/08/2008 and at page 6 of the office action dated 11/14/2008. Applicant has amended claim 42 to require that the agent be added to medium already containing the teleosts. Such a limitation is an obvious change over the teachings of Mizzel and is a matter of design choice. In some circumstances, it would be easier or make logical sense to add the agent to medium already containing the teleosts. For example, when a group of embryos are already in culture media or when many individual embryos are being screened (i.e. high throughput), it is simple to add the agent to the well containing the teleosts. However, at other times, when concentration is needed to be precise or smaller volumes are used, it is logical to add a teleost to culture media already comprising a uniform and precise amount of the agent dispersed. That it

was well-known and obvious to add an agent to the media already containing the teleosts is demonstrated by Blader who adds ethanol and forskolin to teleost embryos already in culture media (page 186, col. 1).

2) The rejection of claims 47-48 and 50-52 under 35 U.S.C. 103(a) as being unpatentable over Mizzel (1997) as applied to claims 42-46 above, and further in view of Terse [1993, Toxicon, 31:913-919] is *withdrawn* in light of Applicant's amendment to claim 42. However, the following new rejection is applied.

Claims 47-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzel (1997) as evidenced by Blader (1998) as applied to claims 42-46, 53 and 57 above, and further in view of Terse [1993, Toxicon, 31:913-919].

The teachings of Mizzell are set forth above. Mizell taught placing each embryo in a single droplet of medium in a single large Petri dish (page 421, col 2, paragraph 4). Mizell did not teach placing each embryo in a well of a multi-well plate (claim 47) wherein the volume of the wells is 300 microliters or less per well (claim 48).

However, Terse et al. taught screening the toxic activity of various mycotoxin agents using 96-well multi-well plates. As evidenced by the specification, standard 96-well plates have a volume of 300 microliters (see page 88, lines 27-29).

However, Terse et al. taught screening the toxic activity of various mycotoxin agents using 96-well multi-well plates. As evidenced by the specification, standard 96-well plates have a volume of 300 microliters (see page 88, lines 27-29).

It would have been obvious to one of skill in the art at the time of filing to combine the teachings of Mizell in screening agents for toxicity using teleosts with the teachings of Terse *et al*,. to carry out an in vivo toxin screen using 96-well microtiter plates. One would have been motivated to combine these teachings because multiwell plates provide a more convenient means of separating samples without cross-

contamination or loss of sample. Terse *et al.* did not specify a volume in which to place the sample in the well, however, in light of the teachings of Mizell using 250µl droplets and the upper volume limit of the wells being 300 µl, one of skill in the art would have been motivated to use a smaller volume of liquid in the multi-well plate to avoid spill over from one well to another and to conserve and to work with smaller amounts of potential toxin. It was obvious to one of skill in the art by looking a teleost embryo, that 200 µl would be more than sufficient to envelope the entire teleost.

One would have a reasonable expectation of success in carrying out a screen as taught by Mizzel using 96-well plates as taught by Terse *et al.* because it was standard in the art to carry out screens in 96-well plates and the multi-well plates are made of a material similar to Petri-dishes and serve the same purpose, only with an added benefit.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

3) The rejection of claim 55 under 35 U.S.C. 103(a) as being unpatentable over Mizell (1997) in view of Maccubbin (1986, Aquatic Toxicology, 9:277-286) or Black (1988, Aquatic Toxicology, 11:129-142) or Marty *et al*, (1990, Aquatic Toxicology, 17:45-62) is *withdrawn* in light of Applicant's amendment to claim 42. However, the following new rejection is applied.

.

Claim 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzel (1997) as evidenced by Blader (1998) as applied to claims 42-46, 53 and 57 above, and further in view of Maccubbin (1986, Aquatic Toxicology, 9:277-286) or Black (1988, Aquatic Toxicology, 11:129-142) or Marty *et al*, (1990, Aquatic Toxicology, 17:45-62).

Claim 55, depending from claim 42, is drawn to a method of screening an agent for toxic activity in vivo comprising administering an agent to a teleost *with a chorion*, and detecting a change in

expression of a protein in a specific organ or tissue of the teleost, a response in the teleost indicating toxic activity in the tissue.

As set forth above, Mizell taught a method for screening an agent for toxic activity in teleosts. Mizell taught administering toxins to zebrafish embryos and detecting toxic effects by monitoring CYP1A activity as an indicator of toxicity. Mizell taught use of dechorionated embryos and did not teach leaving the embryos in the chorion during agent administration.

However, Maccubbin taught a method for screening an agent for toxic activity in rainbow trout, which is a teleost that has a chorion. Maccubbin taught administering 4 different carcinogens (agents) in DMSO to 50-100 (claim 46) embryos *within chorions* and detecting toxic effects by monitoring survival (see para bridging pages 279-280). Maccubbin taught that DMSO, given its widely recognized membrane penetration properties, can facilitate the passage of agents across the chorion, facilitating the screening for toxicity of agents by being a noninvasive technique, not requiring removal of the chorion. Maccubbin taught applying this technique to automate screening and for use in other species.

Similarly, Black taught application of chemicals to trout embryos by the method of Maccubbin and establishes while not all chemicals will be most efficiently transported across the chorion (egg shell), this method has advantages such as being noninvasive and has the ability to be automated and reproducible dose-response toxicity data should be readily obtainable (paragraph bridging pages 137-138).

Additionally, Marty *et al* showed the uptake of a variety of chemicals through the chorion of medaka using radiolabeled chemicals.

It would have been obvious at the time of filing to combine the teleost screening methods of Mizzel with the knowledge of Maccubbin, Black or Marty demonstrating that toxicity of compounds can be tested in teleost embryos with the chorion intact. One of skill in the art would have been motivated to not dechorionate the embryos prior to introducing an agent as it would allow for high throughput,

automated and noninvasive screening. Loss of embryos in the dechorionation process would be prevented and time would be saved.

One would have a reasonable expectation of success in applying the screening techniques of Mizzel to embryos within their chorions as it was demonstrated in the art that many agents do cross the chorion to affect the embryo. While the chorion may offer some protection to the embryo, the art has demonstrated the chorion is not a complete barrier.

Conclusion

No claim is allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632